

Serial No. 10/508,941
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Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1 (original): A method of preparing an amine stereoisomer, which comprises stereoselectively reducing a sulfinylimine that bears on the sulfinyl group a residue of an alcohol, thiol or amine, or reacting a sulfinylimine stereoisomer that bears on the sulfinyl group a residue of an alcohol, thiol or amine with a source of a nucleophile, to afford a sulfinylamine stereoisomer, followed by contacting the sulfinylamine stereoisomer with a reagent suitable for the cleavage of a sulfur-nitrogen bond, to afford an amine stereoisomer.

2 (original): A method as claimed in Claim 1, wherein the sulfinylimine is a sulfinylimine stereoisomer.

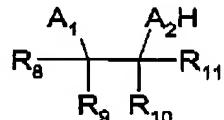
3 (previously presented): A method as claimed in Claim 1, wherein the residue of the alcohol, thiol or amine is in stereoisomeric form.

4 (previously presented): A method as claimed in Claim 1, wherein the residue of the alcohol, thiol or amine is a residue of an optionally N-substituted beta-amino alcohol, thiol or amine.

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5 (original): A method as claimed in Claim 4, wherein the optionally N-substituted beta-amino alcohol, thiol or amine is a compound of the general formula



wherein A₁ is R₇N or (R_{7'})R_{7''}N, R₇ represents hydrogen or -L-R_{7a} in which -L- represents a bond, -CO-, -(CO)O-, -(CO)NR_{7b}-, -SO-, -SO₂-, or -(SO₂)O-, each of R_{7a} and R_{7b} independently represents substituted or unsubstituted alkyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aryl or substituted or unsubstituted heteroaryl, and R_{7'} and R_{7''} are as defined for R_{7a}, or R_{7'} and R_{7''} together with the nitrogen atom to which they are attached and, optionally R₈, form an unsubstituted or substituted heterocyclic group, or R_{7'} together with the nitrogen atom to which it is attached and the carbon atom to which the nitrogen atom is attached forms an unsubstituted or substituted heterocyclic group; A₂ is O, S or NR_{7c} in which R_{7c} is substituted or unsubstituted alkyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aryl or substituted or unsubstituted heteroaryl; and each of R₈, R₉, R₁₀ and R₁₁ is independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aryl or substituted or unsubstituted heteroaryl, or R₈ and R₁₁ together form a substituted or unsubstituted alkylene or heteroalkylene chain.

6 (original): A method as claimed in Claim 5, wherein A₂ is O.

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7 (previously presented): A method as claimed in Claim 5, wherein each of R₈ R₉, R₁₀ and R₁₁ is independently selected from hydrogen, (1-4C)alkyl and phenyl, or the alcohol is selected from (N-methylpyrrolidin-2-yl)diphenylmethanol, quinine, quinidine, hydroquinine, cinchonidine, cinchonine, hydrocinchonidine and ethyl hydrocupreine.

8 (original): A method as claimed in Claim 7, wherein A₁ is R₇N wherein R₇ represents ~SO₂-R_{7a} in which R_{7a} represents (1-6C)alkyl, (6-10C)aryl(1-4C)alkyl or (6-10C)aryl in which any aryl group is unsubstituted or substituted by one, two or three substituents selected independently from halogen, (1-4C)alkyl and (1-4C)alkoxy, or A_{1'} is (R_{7..})R_{7..}N wherein R_{7..} and R_{7..} each independently represents a (1-4C)alkyl group or together with the nitrogen to which they are attached represent a pyrrolidine group that may bear one or two methyl substituents, or the alcohol is selected from (N-methylpyrrolidin-2-yl)diphenylmethanol, quinine, quinidine, hydroquinine, cinchonidine, cinchonine, hydrocinchonidine and ethyl hydrocupreine.

9 (original): A method as claimed in Claim 7, wherein A_{1'} is R₇N and the residue of the alcohol, thiol or amine is a residue of an optionally N-substituted 2-amino-1-phenylpropanol, 2-amino-2-methyl-1-phenylpropanol, 1-amino-1-phenyl-2-propanol, 1-amino-1-phenyl-2-methyl-2-propanol, 1-amino-1-phenyl-2-ethyl-2-butanol, 1-amino-2-indanol, 2-aminoindan-1-ol, 1-amino-2-hydroxy-1,2,3,4-tetrahydronaphthalene or 2-amino-1-hydroxy-1,2,3,4-tetrahydronaphthalene, or A_{1'} is (R_{7..})R_{7..}N and the alcohol is selected from 2-N,N-dimethylamino-1-phenyl-2-propanol, 2-N,N-

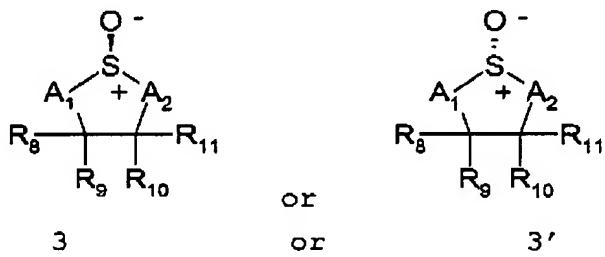
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dibutylamino-1-phenylpropanol, 2-pyrrolidin-1-yl-1-phenylpropanol, 2-(2-methylpyrrolidin-1-yl)-1-phenylpropanol, 2-(2,5-dimethylpyrrolidin-1-yl)-1-phenylpropanol, 2- N,N-dimethylamino-2-methyl-1-phenylpropanol, (N-methylpyrrolidin-2-yl)diphenylmethanol, 1-pyrrolidin-1-ylindan-2-ol, 3-benzyloxy-2-N,N-dimethylamino-1-phenylpropan-2-ol, quinine, quinidine, hydroquinine, cinchonidine, cinchonine, hydrocinchonidine and ethyl hydrocupreine.

10 (previously presented): A method as claimed in Claim 4, wherein the sulfinylimine has been prepared by contacting an iminometal with a 1,2,3-oxathiazolidine-S-oxide, a 1,2,3-dithiazolidine-S-oxide or a 1,2,3-azathiazolidine-S-oxide.

11 (previously presented): A method as claimed Claim 10, wherein the 1,2,3-oxathiazolidine-S-oxide, 1,2,3-dithiazolidine-S-oxide or 1,2,3-azathiazolidine-S-oxide is a compound of formula 3 or 3'



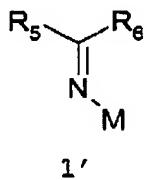
wherein A_1 is R_7N or $(R_{7a})R_{7b}N^+ Q^-$ in which Q^- is an anion, R_7 represents hydrogen or $-L-R_{7a}$ in which $-L-$ represents a bond, $-CO-$, $-(CO)O-$, $-(CO)NR_{7b}-$, $-SO-$, $-SO_2-$, or $-(SO_2)O-$, each of R_{7a} and R_{7b} independently represents substituted or unsubstituted alkyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aryl or substituted or unsubstituted heteroaryl, and R_{7a} and R_{7b} are as defined for R_{7a} , or R_{7a} and R_{7b} together with the nitrogen

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atom to which they are attached and, optionally R_8 , form an unsubstituted or substituted heterocyclic group, or R_7 , together with the nitrogen atom to which it is attached and the carbon atom to which the nitrogen atom is attached forms an unsubstituted or substituted heterocyclic group; A_2 is O, S or NR_{7c} in which R_{7c} is substituted or unsubstituted alkyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aryl or substituted or unsubstituted heteroaryl; and each of R_8 , R_9 , R_{10} and R_{11} is independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aryl or substituted or unsubstituted heteroaryl, or R_8 and R_{11} together form a substituted or unsubstituted alkylene or heteroalkylene chain;

the iminometal is a compound of formula 1'

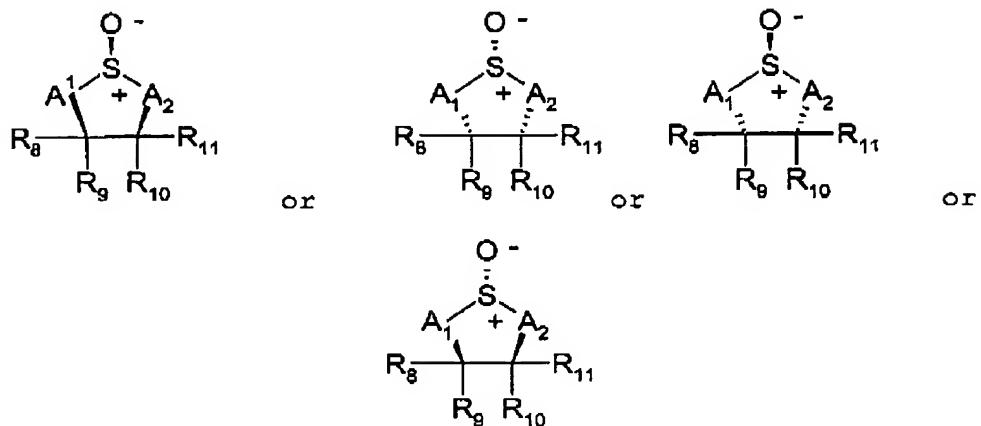


wherein M is CdZ, BaZ, Na, K, MgZ, ZnZ, Li, MnZ, CuZ, TiZ₃ or In and Z is an anion.

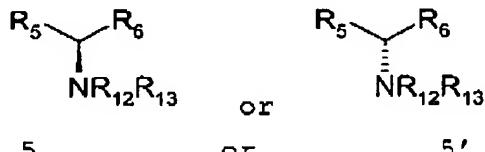
12 (previously presented): A method as claimed in Claim 11, wherein the 1,2,3-oxathiazolidine-S-oxide, 1,2,3-dithiazolidine-S-oxide or 1,2,3-azathiazolidine-S-oxide is a stereoisomer of formula

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13 (previously presented): A method as claimed in Claim 11,
wherein the amine stereoisomer is a compound of formula 5 or
5'

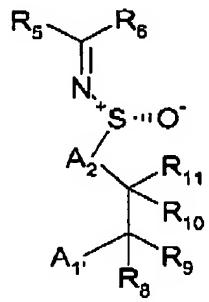


or a pharmaceutically acceptable salt, solvate, clathrate, hydrate or prodrug thereof, wherein R_5 and R_6 are independently substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aralkyl, substituted or unsubstituted aryl or substituted or unsubstituted heteroaryl, or R_5 and R_6 together with the carbon atom to which they are attached form a substituted or unsubstituted cycloalkyl group, and R_{12} and R_{13} together with the nitrogen atom to which they are attached form a heterocycle, or each of R_{12} and R_{13} is independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aralkyl, or substituted or unsubstituted aryl;

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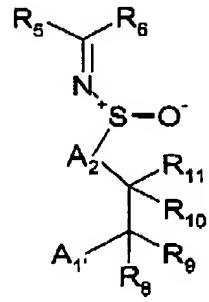
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and the sulfinylimine stereoisomer is a compound of formula 4 or 4'



4

or

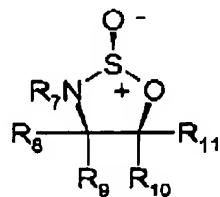


4'

wherein A1' represents R7N or (R7')R7''N.

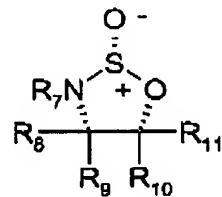
14 (original): A method as claimed in Claim 13, wherein A2 is O.

15 (original): A method as claimed in Claim 14, wherein R5 and R6 are independently substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aralkyl, substituted or unsubstituted aryl or substituted or unsubstituted heteroaryl; the 1,2,3-oxathiazolidine-S-oxide is a compound of the formula 3 or 3'



3

or



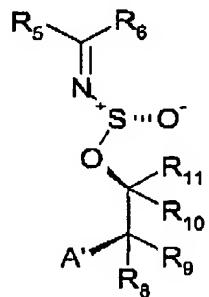
3'

in which R7 represents hydrogen or -L-R7a in which L is a bond or SO2 and R7a is substituted or unsubstituted alkyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aryl

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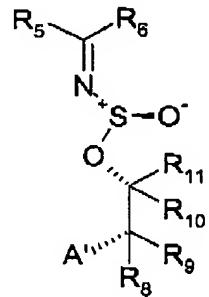
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or substituted or unsubstituted heteroaryl; Z in the iminometal of formula 1' is Cl, Br or I; and the sulfinylimine stereoisomer is a compound of formula



4

or



4'

16 (previously presented): A method as claimed in Claim 13, wherein R₁₂ and R₁₃ are both hydrogen.

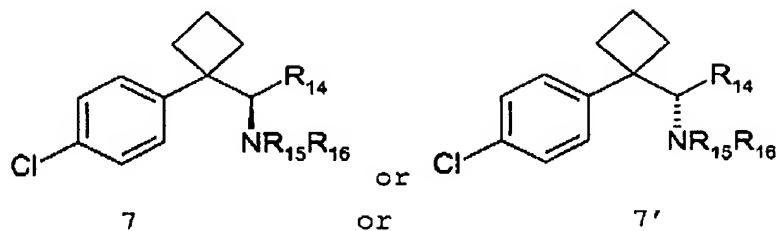
17 (previously presented): A method as claimed in Claim 10, wherein the 1,2,3-oxathiazolidine-S-oxide, 1,2,3-dithiazolidine-S-oxide or 1,2,3-azathiazolidine-S-oxide has been prepared by reacting an optionally N-substituted beta-amino alcohol, thiol or amine with a thionyl halide.

18 (previously presented): A method as claimed in Claim 1, which further comprises the step of alkylating the amine stereoisomer.

19 (previously presented): A method as claimed in Claim 1, wherein the amine stereoisomer is a compound of formula

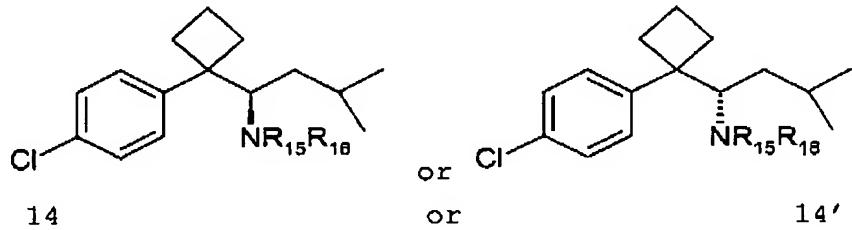
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or a pharmaceutically acceptable salt, solvate, clathrate, hydrate or prodrug thereof, wherein R₁₄ is substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aralkyl or substituted or unsubstituted aryl, and R₁₅ and R₁₆ together with the nitrogen to which they are attached form a heterocycle, or each of R₁₅ and R₁₆ is independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aralkyl or substituted or unsubstituted aryl.

20 (original): A method as claimed in Claim 19, in which the amine stereoisomer is a compound of formula

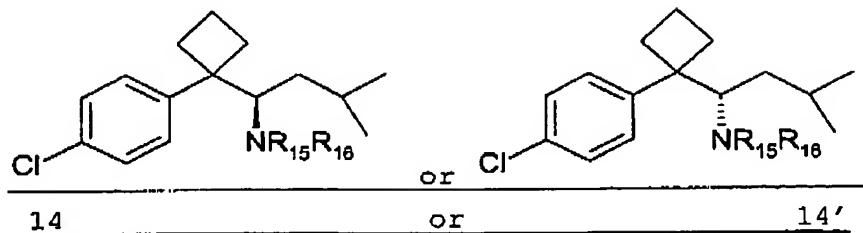


21 (previously presented): A method as claimed in Claim 19, wherein R₁₅ and R₁₆ are both hydrogen.

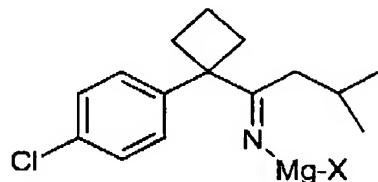
22 (currently amended): A method as claimed in Claim 10 ~~21~~
wherein the amine stereoisomer is a compound of formula

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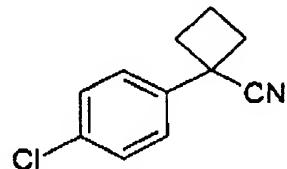
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wherein R_{15} and R_{16} are both hydrogen and the metal imine is a compound of formula



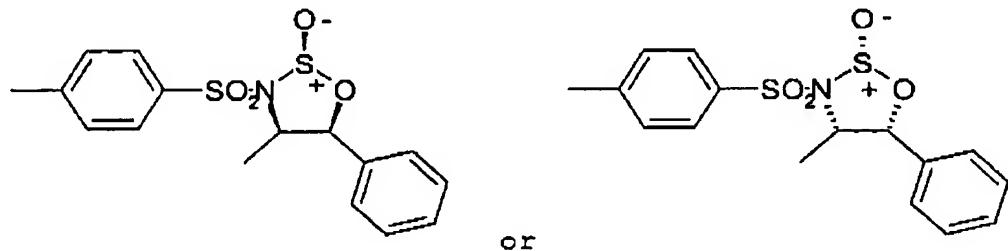
that has been obtained by contacting a compound of formula



15

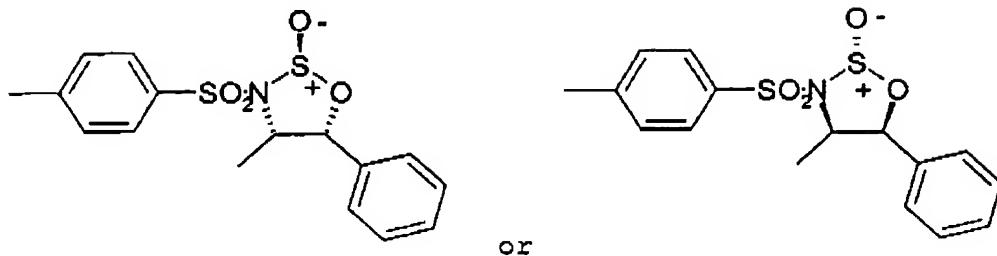
with a compound of formula $i\text{-BuMg-X}$ wherein X is a halogen.

23 (previously presented): A method as claimed in Claim 10, wherein the 1,2,3-oxathiazolidine-S-oxide is a compound of the formula



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24 (previously presented): A method as claimed in Claim 1, wherein the sulfinylimine is reduced using a hydride reducing agent.

25 (original): A method as claimed in Claim 24, wherein the hydride reducing agent is NaBH₄.

26 (previously presented): A method as claimed in Claim 1, in which the reagent suitable for the cleavage of a sulfur-nitrogen bond is an acid.

27 (original): A method as claimed in Claim 26 wherein the acid is HCl.

28 (previously presented): A method as claimed in Claim 1, in which reaction of the sulfinylamine stereoisomer with the reagent suitable for the cleavage of a sulfur-nitrogen bond also affords an optionally N-substituted beta-aminoalcohol, and this optionally N-substituted beta-aminoalcohol is recovered, converted into 1,2,3-oxathiazolidine-S-oxide and recycled.

29 (previously presented): A method as claimed in Claim 1, wherein the stereoselective reduction of the sulfinylimine is performed using a stereoselective reducing agent.

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30 (previously presented): A method as claimed in Claim 1, in which the amine stereoisomer is selected from Alacepril, Benazepril, Benazeprilate, Ceronapril, Cilazapril, Cilazaprilat, Delapril, Enalapril, Enalaprilat, Fasidotril, Fosinopril, Imidapril, Imidaprilat, Libenzapril, Lisinopril, Moexipril, Moexiprilat, Moveltipril, Pentopril, Perindopril, Quinapril, Quinaprilat, Ramipril, Sampatrilat, Spirapril, Spiraprilat, Temocapril, Temocaprilate, Trandolapril, Trandolaprilate, Utibapril, Utibaprilat, Zabicipril, Zabiciprilat, Bucillamine, Penicillamine, Thiamphenicol, Cefprozil, Cephalexin, Cephaloglycin, Cilastatin, Alafosfalin, Ethambutol, Sertraline, Tametraline, Acetylcysteine, Selegiline, Azaserine, Dorzolamide, Colchicine, Dilevalol, Enalapril, Methyldopa, Metaraminol, Acivicin, Melphalan, Ubenimex, Tmsulosin, Tirofiban, Dilevalol, N-dodecyl-N-methylephedrinium, Ofenucine, Tinofedrine, Aceglutamide, l-ephedrine, levopropylhexedrine, (+)-and (-)-Norephedrine, Phenylpropanolamine, Pseudoephedrine, d-farm, (R)-and (S)-Tamsulosin, Dimepheptanol, Lofentanil, Tildine hydrochloride (+)-trans, Ciramadol, Enadoline, Lefetamine, Spiradoline, (+)-Etoxadrol, Levoxadrol, (R)-Amphetamine, Clobenzorex, Dexfenfluramine, Dextroamphetamine, Etilamfetamine, Fenfluramine, Levofenfluramine, Phenylpropanolamine, Cetirizine, (R)- and (S)-Baclofen, (R)- and (S)-Sibutramine, and pharmaceutically acceptable salts thereof.

31 (withdrawn - currently amended): A method as claimed in Claim 1, wherein the sulfinylimine sulfinylamine-stereoisomer is reacted with a source of a nucleophile selected from a nitrile, a Grignard reagent and an organolithium.

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32 (withdrawn - currently amended): A method as claimed in
Claim 31, wherein the sulfinylimine sulfinylamine-stereoisomer
is reacted with a nitrile, and the resultant amine
stereoisomer bearing a nitrile group is hydrolyzed to afford
an amino acid.

33 to 45: (cancelled)